Remarks

Applicant respectfully requests reconsideration. Claims 1, 2, 115-124, 130-156 and 161-169 were pending in this application. By this amendment, claim 123 is cancelled without prejudice or disclaimer. Claims 1, 115, 130, 137, 147 and 162 are amended. Support for these amendments can be found in the specification at least on page 9 lines 4-5, page 12 lines 20-24, page 31 lines 8-17, and claims 1, 142 and 152 as previously pending. As a result, claims 1, 2, 115-122, 124, 130-156 and 161-169 are pending for examination with claims 1, 115, 130, 137, 147 and 162 being independent claims. No new matter has been added.

Rejections under 35 U.S.C. §102

Yeung et al., U.S. Patent No. 5324401:

Claims 1, 2, 130-133, 135-142, 144-146, 149-152, 154-156, 161-165 and 167-169 are rejected under 35 U.S.C. §102(b) as being anticipated by Yeung. Claims 1, 130, 137, 147 and 162 are amended. Applicant respectfully traverses in part.

Yeung has been discussed in the previous response. Briefly, Yeung analyzes polymers using capillary electrophoresis. Capillary electrophoresis involves the migration of polymers according to size and to a lesser extent charge. It is used to physically separate polymers from each other. Each separated polymer migrates through the capillary and is analyzed in its entirety for the presence of a signal. Individual regions of the polymer, including units, plurality of units and/or bound probes, are not sequentially exposed to a station (e.g., an interaction or signal generation station) nor are any signals deriving therefrom sequentially detected.

Yeung does not anticipate the claims as amended for the following reasons:

With respect to claims 1 and 162 (and their dependent claims), Yeung does not distinguish signals of individual units (or unit specific markers) from those arising from linked adjacent units in a single polymer because Yeung analyzes polymers in their entirety. The Examiner previously interpreted the term "adjacent units" broadly, and therefore considered it to embrace units in a physically separate polymer. Claim 1 has been amended to recite linkage of units being detected in a single polymer. Claim 162 has been amended to include the step of distinguishing signals arising from bound labeled unit specific markers and those arising from linked adjacent units of an individual polymer.

With respect to claims 130, 137 and 147 (and their dependent claims), Yeung does not sequentially pass units within a single polymer by a station, nor does Yeung sequentially detect signals arising from linked units in a single polymer. Yeung does not analyze polymers (and their signals) sequentially. Rather Yeung analyzes polymers (and their signals) in their entirety.

Yeung does not teach all the elements of the claims as amended, and therefore it does not anticipate these claims. Reconsideration and withdrawal of the rejection is respectfully requested.

Huang et al., Anal. Chem., 64:2149-54 (1992):

Claims 1, 2, 115, 116, 119-124, 130-134, 137-143, 147-153 and 161 are rejected under 35 U.S.C. §102(b) as being anticipated by Huang. Claims 1, 115, 130, 137 and 147 are amended. Applicant respectfully traverses in part.

Huang has been discussed in the previous response. Briefly, Huang sequences DNA using capillary electrophoresis (discussed above) and a two color detection scheme. Using the Sanger sequencing method and uniquely labeled primers (i.e., JOE and FAM), Huang is able to distinguish between sequencing products having G, T, A and C termini. Huang analyzes the electrophoretically separated sequencing products for the presence of the JOE and/or FAM labels. Each separated nucleic acid migrates through the capillary and is analyzed in its entirety for the presence of a signal. Individual regions of the polymer, including units, plurality of units and/or bound probes, are not sequentially exposed to a station (e.g., an interaction or signal generation station) nor are any signals deriving therefrom sequentially detected.

Huang does not anticipate the claims as amended for the following reasons:

With respect to claim 1 (and its dependent claims), Huang does not distinguish signals of individual units from those arising from linked adjacent units in a single polymer because Huang analyzes sequencing fragments in their entirety. The Examiner previously interpreted the term "adjacent units" broadly, and therefore considered it to embrace units in a physically separate polymer. Claim 1 has been amended to recite linkage of units being detected in a single polymer.

With respect to claims 115, 130, 137 and 147 (and their dependent claims), Huang does not sequentially pass individual units within a single polymer by a station, nor does Huang

sequentially detect signals arising from units in a single polymer. Huang does not analyze polymers (and their signals) sequentially. Rather Huang analyzes polymers (and their signals) in their entirety.

Huang does not teach all the elements of the claims as amended, and therefore it does not anticipate these claims. Reconsideration and withdrawal of the rejection is respectfully requested.

Mank et al., J. of Chromatography A, 708:309-21 (1995):

Claims 115, 117, 118 and 166 are rejected under 35 U.S.C. §102(b) as being anticipated by Mank. Claim 115 is amended. Applicant respectfully traverses in part.

Mank teaches a capillary electrophoresis method for analyzing amino acids and small peptides with derivatized amines. Following derivatization, the amino acids or peptides are separated from each other using capillary electrophoresis. The derivatized products migrate with particular migration times, and can thereby be distinguished from each other. Mank analyzes each derivatized product in its entirety.

Mank does not anticipate the rejected claims because Mank does not sequentially expose derivatized amino acids to a station.

Mank does not teach all the elements of the claims as amended, and therefore it does not anticipate these claims. Reconsideration and withdrawal of the rejection is respectfully requested.

Double Patenting Rejection

Claims 1, 2, 115, 119 and 120 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 13, 14, 19, 22 and 49 of U.S. Patent No. 6403311 to Chan.

Without conceding to the Examiner's position and solely in the interest of expediting prosecution, Applicant has prepared and is in the process of having executed a terminal disclaimer in compliance with 37 CFR 1.321 to overcome the nonstatutory obviousness-type double patenting rejection. In telephone communications on April 17, 2007 with the undersigned, the Examiner stated that an indication in this response that the executed terminal

disclaimer would be forthcoming along with a copy of the unexecuted terminal disclaimer would preclude a finding that Applicant was non-compliant. Submitted herewith are the unexecuted terminal disclaimer and the ownership statement. The executed versions of these documents will be forwarded to the Examiner as soon as they are received by the undersigned.

Once the executed documents are received by the Examiner, reconsideration and withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph

Claims 1, 2, 147 and 148 are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. The Examiner acknowledges that the specification enables identification of individual units of a polymer. The Examiner however states that labeling of each individual unit in a polymer and use of nanochannels is not enabled. Applicant has amended claims 1 and 147 to recite "non-ion conductance signals". Applicant respectfully traverses in part.

An assessment of whether claims are enabled requires an analysis of the Wands factors including the nature of the invention, the breadth of the claims, the state of the art, the relative skill of those in the art, the predictability in the art, the amount of direction provided by the specification, and the presence of working examples. These factors must be taken in their totality in determining if claims are enabled. Moreover, it is the quality and not the quantity of experimentation that must be undue in order to conclude that the claims are not enabled.

The nature of the invention: The invention relates in part to the ability to analyze linearly polymers of linked units. Polymers are linearly passed by one or more stations and signals arising therefrom are sequentially detected. This analysis yields information relating to the location of one or more units in a polymer, and in some instances the distance between units.

The breadth of the claims: Claims 1 and 2 are directed to a method for identifying an individual unit of a polymer by moving the unit relative to a station, detecting a signal arising from this interaction, and distinguishing the signal from signals arising from adjacent units in the polymer. Claims 147 and 148 are directed to a method for analyzing a set of polymers of linked units, orienting the polymers in an electric field, moving the sets of polymers through defined channels including nanochannels, and detecting polymer specific features as the polymers move through the channels.

Quantity of experimentation: The Examiner cites the application on page 64 lines 8-9 for the teaching that "adding *extrinsic* labels to all four bases may cause steric hindrance problems" (emphasis added). However, the paragraph continues "in order to reduce this problem the intrinsic properties of some or all of the nucleotides may be used to label the nucleotides". Therefore, the specification contemplates that signals may be derived from extrinsic labels as well as the intrinsic properties of nucleotides. The rejected claims do not require extrinsic labeling of units, nor do they require signal detection from all units in the polymer. Rather the claims embrace detecting extrinsic and/or inherent signals from at least one individual unit.

The Examiner cites Chan (Mutation Research 2005, 573, p 13-40) as teaching that "a single-base resolution strategy has yet to be articulated with solid-state nanopores". The statement however refers to nanopore sequencing technology which as defined on page 30 first column of the same reference involves discrimination of individual nucleotides by nucleotide-specific ion conductance signals. Claims 1 and 147 have been amended to recite "non-ion conductance signals". In view of these amendments, the teaching of the reference in this regard is no longer relevant.

The unpredictability of the art and the sate of the prior art: The Examiner considers the art unpredictable. The Examiner cites Sauer (J Biotechnology 2001, 86, p181-201) for the teaching that "a complete labeling (100% substitution with fluorescent dNTPs) of all four DNA-bases has not yet to be achieved (sic). Steric hindrance at the polymerase active site is supposed to prevent full replacement of natural dNTPs by the modified analogues." As stated above, the claims do not require extrinsic labeling of all units in the polymer. Rather the claims can be performed using inherent properties of polymer units, and without signal detection from each and every unit in a polymer.

Regarding the practicing of the method of claims 1, 2 and 147 using a nanochannel, the Examiner again cites Chan (Mutation Research 2005, 573, p 13-40). As stated above, the teaching of Chan with regards to nanopore sequencing is moot in view of the amendment to claims 1 and 147 to recite "non-ion conductance signals".

Guidance in the Specification: According to the Examiner, the specification discloses multiple embodiments for the practice of the claimed invention including the method as disclosed in claims 1, 2, 147 and 148. Applicants agree. The specification teaches that signals

may be derived from extrinsic labels as well as inherent properties of polymer units. As stated above, the claimed invention is not limited to extrinsic labeling of all polymer units. The specification further teaches analysis of polymers using nanochannels using methods that are not dependent on ion conductance.

Working Examples: The Examiner states that the specification has no working examples. MPEP §2164.02 states that "The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970)." Moreover, the Wands factors are to be considered in their totality with no one factor being dispositive. In this regard, Applicant considers that a consideration of the Wands factors as a whole supports enablement of the rejected claims (as now amended) even in the absence of a working example.

Conclusion: In view of the foregoing, Applicant maintains that undue experimentation is not required for one of ordinary skill in the art to practice the claimed invention.

Reconsideration and withdrawal of the rejection is respectfully requested.

Conclusion

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed

check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

Maria A. Trevisan
Registration No.: 48,207
WOLF, GREENFIELD & SACKS, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, Massachusetts 02210-2206
(617) 646-8000

Date: April 18, 2007
x04.18.07